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Prevalence and Antibiotic Susceptibility Pattern of Bacterial Pathogens in Intensive Care Unit (ICU) of a Tertiary Care Facility

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Abstract: Aim: To determine the prevalence and antibiotic susceptibility pattern of microorganisms in the ICU patients of a tertiary care facility in Karachi, Pakistan. **Method:** A retrospective study was conducted on the laboratory records of 50 patients with positive culture admitted to a tertiary care facility. A structured questionnaire was used to obtain patients' records comprising of their name, sex, age, diagnosis, sample source, isolated pathogen culture results and antibiotic susceptibility patterns. Blood, tracheal fluid, urine, sputum, pus, peritoneal fluid and catheter tips were included as specimen sources. Total 94% patients selected had clinically suspected nosocomial infections. **Results:** Overall, 45% of them had traumatic brain or spinal injury followed by 35% of post-operative cases, 10% respiratory disease related patients, 6% cardiac patients, 2% renal failure and 2% with miscellaneous infections. Majority of the patients admitted to the ICU were in the age range 51- 65 years. Positive microbial growth samples included blood (30%), trachea (24%), urine (26%), sputum (10%), pus (4%), peritoneal fluids (2%) and catheter tip (4%). Amongst the samples tested, *Acinetobacter spp.* (22%) were predominant, followed by *E. coli* (14%), *P. aeruginosa* (10%), *S. aureus* (10%) and *Enterococcus spp.* (8%). Majority of the gram negative species were resistant to amoxiclave, cefotaxime, pipercillin and teicoplanin. **Conclusions:** The incidence of nosocomial infections is high in ICU patients. Thus accurate antimicrobial treatment strategies together with the development of new therapeutic regimens and risk assessment in hospitals and their ICUs is significantly required to prevent antimicrobial drug resistance among microorganisms.

Keywords: Broad-Spectrum Antibiotics, Intensive Care Unit, Nosocomial Infections

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Introduction

Nosocomial infections develop in patients who are admitted to a healthcare facility or are under a medical care. Centre for Disease Prevention and Control (CDC) defines hospital acquired infections (HAIs) that develops at least 48–72 hours after hospital admittance [1]. According to World Health Organization (WHO), nearly 15% of all hospitalized patients suffer from nosocomial infections during their stay at hospital as they are exposed to a variety of microorganisms through diverse sources like healthcare personnel, infected patients and surrounding environment [2]. Wide-ranging infection control and monitoring measures are regularly implemented in many countries, yet intensive care unit (ICU) is a budding cause of nosocomial infections [3].

Multi-drug resistant (MDR) nosocomial infections or HAIs are the most prominent reasons of mortality and morbidity in hospitalized patients [4]. These multi-drug resistant infections are

considered as substantial economic burden, not only on the patients but also on the health care system of any country [5]. Antibiotic resistance is a global health concern, predominantly affecting developing nations, including Pakistan [6]. Antibiotic misuse and overuse partially because of irrationally prescribed antibiotic therapy, improper diagnosis and wrong antibiotic combinations due to erroneous prescription or reduced compliance are all major reasons to the extensive drug resistance surrounded by the HAIs [7].

HAIs are developed with the use of devices used in medical procedures e.g., ventilators, central lines used in blood stream and catheters [2]. According to CDC classification, HAI infections include Ventilator-Associated Pneumonia (VAP), Surgical Site Infections (SSI), Central Line-Associated Bloodstream Infections (CLABSI) and Catheter-Associated Urinary Tract Infections (CAUTI) [2]. Among these types, three main kinds of infections makes up for greater than 60% of all HAIs namely pneumonia (generally ventilator-associated), primary bloodstream infection (generally linked with the use of an intravascular device) and urinary tract infections (frequently catheter associated) [8].

Globally, ICUs encounter increasingly rapid spread and emergence of antimicrobial resistant bacteria as a result of recurrent use of broad-spectrum antimicrobials [9-12]. In addition, microbial strains and their sensitivity to antibiotics is variable in ICUs. Understanding and precise information about integral bacterial disease causing microorganisms and their resistance pattern aids in managing ICU patients [13]. Most of the patients admitted to an ICU cannot afford to wait for culture-sensitivity reports to arrive and then to begin treatment with an antimicrobial drug. Thus, reporting the common organisms in ICU and their susceptibility to antimicrobials is essentially required so that the prescribed antimicrobial drugs can produce optimum results. Furthermore, aforesaid information helps to formulate recommendations for prescribing antimicrobials and enable the prescriber to follow a specific treatment protocol [14].

Therefore, this study aims to identify the pre-dominant isolated bacterial microbes and their drug resistance pattern for patients admitted to ICU of tertiary care private hospital established in Karachi, Pakistan.

Methodology

Patient Data Collection

A retrospective study was carried out on laboratory records of 50 positive culture patients admitted at ICU of a tertiary care facility for a time period of 2 months during the year 2020. A structured questionnaire was used to obtain patients' records comprising of their name, gender, age, diagnosis, sample source, isolated pathogen culture results, antibiotic sensitivity and resistance patterns. Prescribed drugs for ICU cultures were confirmed using the prescription in subsequent patient profiles.

Inclusion and Exclusion Criteria

The inclusion criteria include those ICU patients who have acquired nosocomial infections after 48hrs of ICU admission or within 48hrs of ICU transfer. The study excludes patients spending less than 48hrs in the ICU. Patients who acquire nosocomial infection after admission to the hospital after 48hrs and then transferred to ICU were also excluded from the study.

Specimen Collection for Microbial Analysis

Specimen sources included blood, tracheal fluid, urine, sputum, pus, peritoneal fluid and catheter tip. The samples were collected under aseptic condition at the patient bed side and then transferred to microbiology lab immediately for process.

Antibiotic Susceptibility Profile

The following guidelines of the National Committee for Clinical Laboratory Standards [15], Kirby-Bauer disk diffusion method were used to test antimicrobial sensitivity in Mueller-Hinton agar medium. The microbial cultures were tested against the antibiotics i.e. Amikacin, Amoxclav, Azteronem, Cefotaxime, Ceftriaxone, Co-trimaxazole, Ciprofloxacin, Gentamicin, Imipenem, Levofloxacin, Meropenem, Pipercillin and Teicoplanin.

Results

Study Population

A total of 50 ICU patient records were selected based on inclusion criteria of patients, of which 94% patients had clinically suspected nosocomial infections. Around 45% of the patients have traumatic brain or spinal injury due to road traffic accidents followed by 35% of post-operative cases, 10% of respiratory disease related patients, 6% of cardiac patients, 2% of renal failure and 2% miscellaneous infections (Figure 1). Maximum patients admitted into the ICU were between the age range of 51- 65 years (38%) followed by 65- 80 years (32%), 21-35 years (12%), 36-50 years (10%) and 81-95 years (8%) (Table 1).

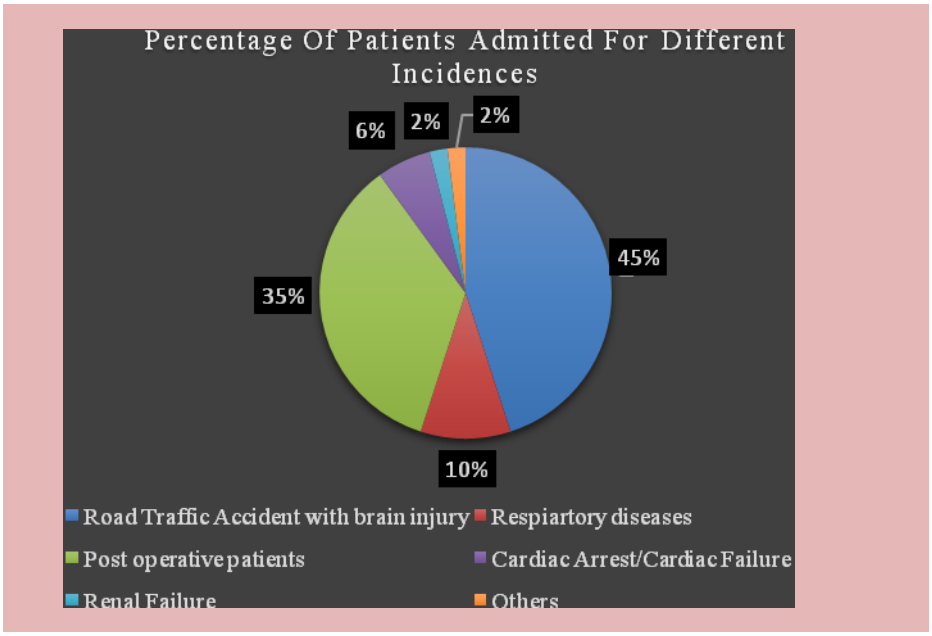

Figure 1: Distribution of patients according to different diseases.

Table 1: Age and sex of patients vs Number of cases.

Patient demographics		
Age in years	**Cases (N)**	**N (%)**
21 - 35	6	12
36 - 50	5	10
51 - 65	19	38
65 - 80	16	32
81 - 95	4	8
Sex		
Female	25	50
Male	25	50

Pathogens Isolated

Among the samples analyzed for the microbial analysis, the positive growth samples included blood (30%), trachea (24%), urine (26%), sputum (10%), pus (4%), peritoneal fluids (2%) and catheter tip (4%), as shown in Table 2. Amongst the bacteria isolated, *Acinetobacter* species (22%) had the highest prevalence (Table 3), followed by *E. coli* (14%), *P. aeruginosa* (10%), *S. aureus* (10%), Enterococcus species (8%), *S. pneumoniae* (6%), *K. oxytoca* (4%), *Enterobacter* species (2%), *Bacillus* species (2%), *Burkholderia* species (2%).

Table 2: Distribution of microorganisms in samples isolated from ICU patients.

S. No	Source of Sample	N (% Isolate)
1	Blood	15 (30%)
2	Trachea	12 (24%)
3	Urine	13 (26%)
4	Sputum	5 (10%)
5	Pus	2 (4%)
6	Peritoneal fluid	1 (2%)
7	Catheter Tip	2 (4%)

Table 3: Microorganisms isolated from samples of ICU patients.

Bacterial isolates	Samples							
	Blood	Tracheal	Urine	Pus	Sputum	Peritoneal fluid	Catheter tip	Total %
***Bacillus* species**	1 (2%)	-	-	-	-	-	-	1 (2%)
Enterobacter	-	-	1(2%)	-	-	-	-	1 (2%)
Esherichia coli	-	-	7(14%)	-	-	-	-	7 (14%)
Klebsiella oxytoca	1(2%)	-	1(2%)	-	-	-	-	2 (4%)
Streptococci D	-	-	1(2%)	-	-	-	-	1 (2%)
Streptococcus pneumoniae	3(6%)	-	-	-	-	-	-	3 (6%)
Pseudomonas aeruginosa	-	1(2%)	-	3(6%)	1(2%)	-	-	5 (10%)
Staphylococcus aureus	1(2%)	2(4%)		1(2%)	-	-	-	5 (10%)
***Acinetobacter* species**	2(4%)	6(12%)	1(2%)	1(2%)	-	-	1(2%)	11(22%)
Burkholderia species	-	-	1(2%)	-		-	-	1 (2%)
***Enterococcus* species**	-	1(1%)	2(4%)	-	-	1(2%)	-	4 (8%)

Antibiotic susceptibility profile

Antibiotic susceptibility profile of the common gram negative isolates is depicted in Table 4. The group of drugs utilized in the study showed susceptibility pattern for ciprofloxacin (78.31%) and levofloxacin (78.61%) against *Enterobacter* species. respectively. Isolates of *Enterobacter* were

highly sensitive to carbapenams including meropenam (100%) and Imipenem (81.22%). Quinolones was found to be the second most potent antimicrobial used for the treatment of *Enterobacter* infections. Co-trimoxazole combination was also found to be highly effective against *Enterobacter species* (75.35%) followed by Aminoglycosides including amikacin (55.64%) and gentamicin (57.62%). Enterobacter species were found to be resistant against Cephalosporin's including cefotaxime and ceftriaxone.

E. coli isolates were highly sensitive to Levofloxacin (100%), Co-trimoxazole (92.36%), Ceftriaxone (98.17%), Ciprofloxacin (80.22%), Gentamicin (85.29%), Amikacin (85.63%), Imipenem (82.81%) and Aztreonam (84.23%). Whereas, *Pseudomonas aeruginosa* isolates were sensitive to Ciprofloxacin (93.18%), Gentamicin (92.68%), Amikacin (90.21%), levofloxacin (92.27%) and only 66.24% sensitive to Pipercillin.

Klebsiella species isolated showed sensitivity to Imipenem (100%), Meropenam (100%), Levofloxacin (91.28%), Co-trimoxazole (77.34%), Ciprofloxacin (88.21%), and Gentamicin (74.52%) Amikacin (74.26%) and Ceftriaxone (73.12%). *Acinetobacter* isolates were highly sensitive to Imipenem (100%), and Meropenam (71.12%). Majority of the gram- negative species were found to be resistant to Amoxiclave, Cefotaxime, Pipercillin and Teicoplanin.

Table 4: Antibiotic susceptibility profile (%) among the most frequent Gram negative bacteria isolated from ICU patients.

Antibiotic	**Bacterial isolates**				
	Enterobacter species	***Escherichia coli***	***Pseudomonas aeruginosa***	***Klebsiella* species**	***Acinetobacter* species**
Amikacin	55.64	85.63	90.21	74.26	43.54
Amoxclav	0	0	0	0	0
Azteronem	15.22	84.23	50.37	34.8	7.2
Cefotaxime	0	0	0	0	0
Ceftriaxone	18.6	98.17	0	73.12	8.24
Co-trimaxazole	75.35	92.36	0	77.34	20.48
Ciprofloxacin	78.31	80.22	93.18	88.21	30.46
Gentamicin	55.62	85.29	92.68	74.52	44.2
Imipenem	81.22	82.81	74.25	100	100
Levofloxacin	78.61	100	92.27	91.28	13.54
Meropenem	100	65.24	70.25	100	71.12
Pipercillin	29.78	0	66.24	34.55	42.57
Teicoplanin	25.32	0	0	0	0

Discussion

Multi drug resistant Gram negative and positive bacterial species comprising *Enterobacteriaceae,* a wide range of *Pseudomonas*, *Acinetobacter* and *Staphylococcus* species count for up to 70% of the healthcare associated infections in hospitalized ICU patients [1]. Bacteria are similarly spread between ICU patients through infected respiratory secretions and by other non-living objects in the ICU setting [16, 17]. It has been estimated that approximately 20% of ICU patients in European intensive care units develop nosocomial infections, frequently initiated by resistant bacterial strains [18]. A study carried out in Maiduguri Teaching Hospital has reported 38.4% cases of nosocomial microbes that encompassed various healthcare wards including the ICU [19]. Around 70.0% of them were positive for bacterial growth.

Amongst ICU patients the rates of nosocomial infections range from 5% - 30% and account for 20% to 25% of all infections, though ICU beds are ~5% of total hospital beds [20]. The greater

risk of infections is directly related to the severity of the patient's disease, extent of exposure to invasive procedures and devices, length of stay and increased contact with the healthcare personnel [20]. Infectious complications related therapeutic mediations include immunosuppressive therapy, catheters, life support system, intravenous fluid treatments and the broad use of antibiotics [21]. In addition, infectious patients' ICU mortality is twice as high as that of non-infected patients [22]. In 2007, an International Infection Study on ICU found that patients with extended ICU stays had a greater risk of infection, particularly due to resistant species of *Staphylococci, Pseudomonas, Acinetobacter* and the yeast *Candida* [3].

The incidence of infections acquired by ICUs is considerably higher in developing nations than in developed countries, ranging amid of 4.4% and 88.9% [23]. In low- and middle-income countries (LMICs) antimicrobial resistance and its aftermaths are more devastating as the prevalence of infectious diseases is significantly high in these countries. Correspondingly, it becomes highly challenging to prevent infection and execute effective control strategies [24]. Pakistan currently has no monitoring program at the indigenous level to guide stakeholders on the actual prevalence of antibiotic resistance [25].

This study estimated the incidence and patterns of antimicrobial susceptibility against the microbial isolates from ICU patients. However, frequently isolated pathogens were gram-negative including *Acinetobacter species* followed by *Escherichia coli* and *Pseudomonas aeruginosa*. These findings were alike as described by Akpaka et al., 2008 and Orrett 2004 [19, 26]. Many other factors may have caused the high incidence rates of these organisms including but not limited to the following *e.g.,* the use of extended assisted ventilation procedures in ICU, prolonged endotracheal intubations and central venous catheterization in ICU patients. Moreover, supplementary factors such as microbial cross contamination through health care staff, and environmental contamination and also via infected patients etc. [27].

Situational analysis shows that the microbial isolation requires timely and appropriate identification of disease causing pathogens involved in development of healthcare associated infections [19]. Clinical correlation with microbiological sensitivity results are hence play significant role in accurate selection of antimicrobials according to patient condition.

Acinetobacter species are widely present in blood, trachea, catheter tip and urine, because of which their prevalence rate is the highest in current study. *Acinetobacter* colonization in ICU may have originated under the pressure of antibiotics from the patients' own flora, contaminated hospital equipment and the hands of healthcare personals [28]. The high prevalence of *Acinetobacter* species in ICU patients warrant the risk of developing multi-drug resistant bacteria that may become difficult to treat. *Acinetobacter* isolates were found to be drug resistant to majority of antimicrobial drugs excluding carbapenams.

A high percentage of *Escherichia coli* in urine samples were identified. The reason behind is the prolonged use of urinary catheters in ICU patients. It was also identified that the carbapenams, imipenem and meropenam, are highly effective for the treatment of *Enterobacteriaceae* family including *Enterobacter species* and *Escherichia coli* that is in accordance to results reported by Turner (1999) and Akapaka et al., (2008) [19, 29]. In 2012, a study conducted in Odisha demonstrated 28.2% rate of nosocomial infections, predominantly of which includes Urinary tract infections [30]. The main isolate was *E. coli* (52.7%) followed by *P. mirabilis* (15.4%), *P. aeruginosa* (13.2%), *C. albicans* (6.6%), *S. aureus* (5.5%), *K. pneumoniae* (3.3%) and *E. faecalis* (2.2%). It was also discovered that *E. coli* was vastly susceptible to Polymyxin B, Ceftriaxone and Gatifloxacin and highly resistant to Cefadroxil, Cephalexin, Prulifloxacin and Tobramycin [30].The susceptibility rates noted for *P. aeruginosa* were for quinolones (ciprofloxacin and levofloxacin) and for aminoglycoside antibiotic drugs (gentamicin and amikacin). This is in accordance to a study conducted in USA on gram negative bacteria among ICU patients and in Uganda [1, 31]. The most frequently isolated microorganisms in a study conducted in an ICU of teaching hospital in northwest of Iran were found to be *E. coli* (16.7%), *P. aeruginosa* (7.5%) and

E. aerogenes (50.6%). *S. aureus* was the predominant pathogen amongst gram-positives (39.7%). Multidrug-resistant (MDR) gram-negative bacteria were recorded including 20% *Klebsiella*, 16.6% Pseudomonas and 25.8% Acinetobacter. Methicillin-resistant *S. aureus* (MRSA) was found to be 87.5%. The most effective antimicrobials were found to be vancomycin (93.5%) followed by gentamicin (46%) and amikacin (71.5%). Generally, the sensitivity pattern to antibiotics was found to be ciprofloxacin (36%), trimethoprim sulfamethoxazole (20%), ceftazidime (20.5%), imipenem (19%), and ceftriaxone (12%) [32].

There was a close association between development of nosocomial infections within 48 hours of admission in ICU due to use of indwelling catheters and intubations, assisted ventilation through ventilators and surgical site infections, thus, the patients with severe brain and spinal injury has a higher risk of developing healthcare associated infections [1].

We are currently encountering multi-drug resistant bacteria which are problematic to treat due to development resistant strains of bacteria. The incredible therapeutic benefit offered by antimicrobials is being susceptible by the emergence of resistant strains of bacteria and associated pathogenic organisms. This problem has recently been aggravated due to progressive rise in development of multi-resistant strains thereby limiting antibiotic development and discovery programs [24]. Also the attitude and practices in prevention and control of HAIs need to be addressed along with the implementation of antimicrobial stewardship programs [33, 34].

Conclusions

The most frequent bacterial isolates were *Acinetobacter* species and *Escherichia coli* in ICU patients. Thus, empirically when the antibiotic is selected for treatment of health care associated infections it should be effective against these microorganisms. The duration of ICU stay in hospital is directly proportional to the risk of development of HAIs in ICU patients. The continued use of indwelling catheters and devices require cautious prophylactic protocols of microbiological monitoring. Both antimicrobial resistance and reduction in health care associated infections has now become a goal of all healthcare facilities including ICU's. Stringent infection control methods like practicing comprehensive safety measures, constant antibiotic surveillance activities and rigorous observance to hand washing practices are required for the said purpose. Henceforth, proper and accurate antimicrobial utilization along with the risk assessment of ICUs is fundamental to avoid the incidences of multi-drug resistance bacteria.

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